WHAT IS CLAIMED IS:

**1.** A conjugate exhibiting interferon β activity, which conjugate comprises at least one first non-polypeptide moiety covalently attached to an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by at least one introduction and at least one removal of an amino acid residue, which amino acid residue comprises an attachment group for the first non-polypeptide moiety.

**2.** The conjugate of claim 1, wherein the first non-polypeptide moiety is selected from the group consisting of: a polymer molecule, a lipophilic compound, a sugar moiety and an organic derivatizing agent.

**3.** The conjugate of claim 2, wherein the polymer molecule comprises linear or branched polyethylene glycol.

**4.** The conjugate of claim 1, wherein the first non-polypeptide moiety comprises a polymer molecule having an attachment group selected from the group consisting of: lysine, aspartic acid, glutamic acid and cysteine.

**5.** The conjugate of claim 4, wherein the first non-polypeptide moiety is a polymer molecule having lysine as an attachment group.

**6.** A conjugate exhibiting interferon β activity, which conjugate comprises at least one first non-polypeptide moiety conjugated to at least one lysine residue of an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by at least one introduction or removal of a lysine residue.

**7.** The conjugate of claim 6, which interferon β polypeptide variant differs from a wild-type human interferon β by introduction and removal of a lysine residue.

**8.** The conjugate of claim 6, wherein the lysine residue removed is selected from one or more residue selected from the group consisting of: K19, K33, K45, K52, K99, K105, K108, K115, K123, K134 and K136.

**9.** The conjugate of claim 8, wherein the lysine residue has been substituted with an arginine or a glutamine residue.

**10.** The conjugate of claim 6, wherein the interferon β polypeptide variant comprises one of the following sets of mutations:

K19R+K45R+K123R;
K19Q+K45R+K123R;
K19R+K45Q+K123R;
K19R+K45R+K123Q;
K19Q+K45Q+K123R;
K19R+K45Q+K123Q;
K19Q+K45R+K123Q;
K19Q+K45Q+K123Q;
K45R+K123R;
K45Q+K123R;
K45Q+K123Q;
K45R+K123Q;
K19R+K123R;
K19Q+K123R;
K19R+K123Q;
K19Q+K123Q;
K19R+K45R;
K19Q+K45R;
K19R+K45Q;
K19Q+K45Q;
K52R+K134R;
K99R+K136R;
K33R+K105R+K136R;
K52R+K108R+K134R;
K99R+K115R+K136R;
K19R+K33R+K45R+K123R;
K19R+K45R+K52R+K123R;
K19R+K33R+K45R+K52R+K123R; or
K19R+K45R+K52R+K99R+K123R.

**11.** The conjugate of claim 6, wherein a lysine residue has been introduced in a position selected from the group consisting of: N4, F8, L9, R11, S12, F15, Q16, Q18, L20, W22, Q23, G26, R27, L28, E29, Y30, L32, R35, M36, N37, D39, P41, E42, E43, L47, Q48, Q49, T58, Q64, N65, F67, A68, R71, Q72, D73, S75, S76, G78, N80, E81, I83, E85, N86, A89, N90, Y92, H93, H97, T100, L102, E103, L106, E107, E109, D110, F111, R113, G114, L116, M117, L120, H121, R124, G127, R128, L130, H131, E137, Y138, H140, I145, R147, V148, E149, R152, Y155, F156, N158, R159, G162, Y163, R165 and N166 of SEQ ID NO 2.

**12.** The conjugate of claim 11, wherein the interferon β polypeptide variant comprises at least one substitution selected from the group consisting of: N4K, R11K, G26K, R27K, Q48K, Q49K, R71K, D73K, S75K, E85K, A89K, Y92K, H93K, F111K, R113K, L116K, R124K, G127K and Y155K.

**13.** The conjugate of claim 12, wherein the substitution is selected from the group consisting of: Q49K and F111K.

**14.** The conjugate of claim 6, comprising at least two introduced lysine residues.

**15.** The conjugate of claim 11, wherein the interferon β polypeptide variant further comprises the removal of at least one lysine residue.

**16.** The conjugate of claim 15, wherein the at least one lysine residue is selected from the group consisting of: K19, K33, K45, K52, K99, K105, K108, K115, K123, K134 and K136.

**17.** The conjugate of claim 15, comprising one of the following sets of mutations:

K19R+K45R+F111K+K123R;
K19R+K45R+Q49K+F111K+K123R;
K19R+K45R+Q49K+K123R;
K19R+K45R+ F111K;
K19R+K45R+Q49K+F111K;
K19R+Q49K+K123R;
K19R+Q49K+F111K+K123R;
K45Q+F111K+K123Q;
K45R+Q49K+K123R; or
K45R+Q49K+F111K+K123R.

**18.** The conjugate of claim 1 or 6, wherein the non-polypeptide moiety comprises a polymer selected from the group consisting of: SS-PEG, NPC-PEG, aldehyd-PEG, mPEG-SPA, PEG-SCM and mPEG-BTC.

**19.** A conjugate exhibiting interferon β activity, which conjugate comprises at least one first non-polypeptide moiety conjugated to at least one cysteine residue of an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild type interferon

β polypeptide by the introduction of at least one cysteine residue at a position selected from the group consisting of: F8, L9, R11, S12, F15, Q16, Q18, L20, W22, L28, L32, M36, P41, T58, Q64, N65, F67, I83, E85, N86, A89, N90, Y92, H93, H97, T100, L102, E103, L106, M117, L120, H121, R124, G127, R128, L130, H131, H140, I145, R147, V148, E149, R152, Y155, and F156 of SEQ ID NO 2.

**20.** The conjugate of claim 19, wherein the interferon β polypeptide variant further comprises removal of at least one cysteine residue.

**21.** The conjugate of claim 20, wherein the cysteine residue removed comprises C17.

**22.** The conjugate of claim 19, wherein the interferon β polypeptide variant comprises at least one of the mutations C17S or N80C.

**23.** The conjugate of claim 19, wherein the interferon β polypeptide variant comprises the mutations C17S and N80C.

**24.** The conjugate of claim 19, wherein the first non-polypeptide moiety is a polymer molecule.

**25.** A conjugate exhibiting interferon β activity, which conjugate comprises at least one first non-polypeptide moiety having an acid group as an attachment group, which moiety is conjugated to at least one aspartic acid or glutamic acid residue of an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by at least one introduction or removal of an aspartic acid or a glutamic acid residue.

**26.** The conjugate of claim 25, wherein at least one amino acid residue selected from the group consisting of: N4, L5, L6, F8, L9, Q10, R11, S12, S13, F15, Q16, Q18, K19, L20, W22, Q23, L24, N25, G26, R27, Y30, M36, Q46, Q48, Q49, I66, F67, A68, I69, F70, R71, S75, T82, I83, L87, A89, N90, V91, Y92, H93, Q94, I95, N96, H97, K108, F111, L116, L120, K123, R124, Y126, G127, R128, L130, H131, Y132, K134, A135, H140, T144, R147, Y155, F156, N158, R159, G162, Y163 and R165 of SEQ ID NO 2 is substituted with an aspartic acid residue or a glutamic acid residue.

**27.** The conjugate of claim 25, comprising introduction of at least two introduced aspartic acid or glutamic acid residues.

**28.** The conjugate of claim 25, comprising at least two first non-polypeptide moieties.

**29.** The conjugate of claim 25, wherein the first non-polypeptide moiety is a polymer molecule.

**30.** The conjugate of claim 29, wherein the second non-polypeptide moiety comprises a sugar moiety.

**31.** The conjugate of claim 34, wherein the amino acid sequence of the interferon β polypeptide variant further comprises at least one of an introduction or a removal of an *in vivo* glycosylation site.

**32.** The conjugate of claim 31, wherein the first non-polypeptide moiety is a polymer molecule having lysine as an attachment group.

**33.** The conjugate of claim 1, 6, 19 or 25, which conjugate comprises a second non-polypeptide moiety.

**34.** The conjugate of claim 33, wherein the polypeptide comprises at least one removed amino acid residue comprising an attachment group for the first non-polypeptide moiety, and at least one introduced amino acid residue comprising an attachment group for the second non-polypeptide moiety.

**35.** The conjugate of claim 33, wherein the amino acid sequence of the interferon β polypeptide variant comprises at least two removed amino acid residues comprising attachment groups for the first non-polypeptide moiety and at least one introduced amino acid residue comprising an attachment group for the second non-polypeptide moiety.

**36.** The conjugate of claim 33, wherein the second non-polypeptide moiety comprises a sugar moiety.

**37.** A conjugate exhibiting interferon β activity, which conjugate comprises at least one polymer molecule and at least one sugar moiety covalently attached to an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by

(a) at least one introduction or removal of an amino acid residue, which amino acid residue comprises an attachment group for the polymer molecule, and

(b) at least one introduction or removal of an amino acid residue, which amino acid residue comprises an attachment group for the sugar moiety,

with the proviso that when the attachment group for the polymer molecule is a cysteine residue, and the sugar moiety is an N-linked sugar moiety, introduction of a cysteine residue does not destroy an N-glycosylation site.

**38.** The conjugate of claim 37, wherein the polymer molecule has lysine as an attachment group.

**39.** The conjugate of claim 38, wherein the polypeptide variant comprises at least one removed amino acid residue comprising an attachment group for the first non-polypeptide moiety and at least one introduced amino acid residue comprising an attachment group for the second non-polypeptide moiety.

**40.** The conjugate of claim 37, wherein the interferon β polypeptide variant comprises one of the following sets of mutations:

K19R+K45R+Q49N+Q51T+F111N+R113T+K123R;
K19R+K45R+Q49N+Q51T+F111N+R113T; or
K19R+K45R+Q49N+Q51T+ K123R.

**41.** The conjugate of claim 1, 6, 19, 25 or 37, wherein the interferon β polypeptide variant comprises a modified N-terminus, which modified N-terminus is unavailable for conjugation to a non-polypeptide moiety.

**42.** A conjugate exhibiting interferon β activity, which conjugate comprises an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by introduction of at least one glycosylation site, the conjugate further comprising at least one un-PEGylated sugar moiety attached to the introduced glycosylation site.

**43.** A conjugate exhibiting interferon β activity, which conjugate comprises an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by at least one introduction or removal of a glycosylation site by introducing or removing one or more amino acid residues comprising a glycosylation site in a position that is occupied by an amino acid residue having at least 25% of its side chain surface exposed in wildtype human interferon β.

**44.** The conjugate of claim 42 or 43, wherein the interferon β polypeptide variant comprises at least one mutation selected from the group consisting of: S2N+N4T, L9N+R11T, R11N, S12N+N14T, F15N+C16S, Q16N+Q18T, K19N+L21T, Q23N+H25T, G26N+L28T, R27N+E29T, L28N+Y30T, D39T, K45N+L47T, Q46N+Q48T, Q48N+F50T, Q49N+Q51T, Q51N+E53T, R71N+D73T, Q72N, D73N, S75N, S76N+G78T, L88T, Y92T, N93N+I95T, L98T, E103N+K105T, E104N+L106T, E107N+E109T, K108N+D110T, D110N, F111N+R113T and L116N.

**45.** The conjugate of claim 44, wherein the interferon β polypeptide comprises one of the following sets of substitutions: Q49N+Q51T; Q49N+Q51T+F111N+R113T; or Q49N+Q51T+R71N+D73T+F111N+R113T.

**46.** The conjugate of claim 42 or 43, wherein the amino acid sequence further differs by removal of an amino acid comprising a glycosylation site.

**47.** The conjugate of claim 46, wherein the glycosylation site comprises an N-glycosylation site.

**48.** A conjugate exhibiting interferon β activity, which conjugate comprises a sugar moiety covalently attached to an interferon β polypeptide variant, which interferon β polypeptide variant differs from a wild-type human interferon β by removal of at least one glycosylation site.

**49.** The conjugate of claim 43 or 48, wherein an N-glycosylation site is removed by the mutation N80C.

**50.** The conjugate of claim 1, 6, 19, 25, 37 or 43, wherein the interferon β polypeptide further comprises at least one substitution in a position selected from among M1, C17, N80 or V101.

**51.** The conjugate of claim 50, wherein the interferon β polypeptide variant comprises at least one substitution selected from M1del, M1K or C17S.

**52.** A nucleotide sequence encoding an interferon β polypeptide variant, which interferon β polypeptide variant comprises component of a conjugate exhibiting interferon β activity.

**53.** A host cell comprising the nucleotide sequence of claim 52.

**54.** An expression vector comprising the nucleotide sequence of claim 52.

**55.** A host cell comprising the expression vector of claim 54.

**56.** The host cell of claim 53 or 55, which host cell comprises a CHO cell, a BHK cell, a HEK293 cell or an SF9 cell.

**57.** A method of reducing immunogenicity or increasing functional *in vivo* half-life or serum half-life of an interferon β polypeptide variant, the method comprising:

(a) introducing an amino acid residue comprising an attachment group for a first non-polypeptide moiety into a position exposed at the surface of an interferon β polypeptide that does not contain such group; or

(b) removing an amino acid residue comprising an attachment group for the first non-polypeptide moiety; and

conjugating the interferon β polypeptide variant with the first non-polypeptide moiety.

**58.** The method of claim 57, wherein the non-polypeptide moiety is selected from the group consisting of a polymer molecule, a sugar moiety, a lipophilic group and an organic derivatizing agent.

**59.** A method for preparing a conjugate exhibiting interferon β activity, the method comprising:

contacting an interferon β polypeptide variant with a first non-polypeptide moiety under conditions conducive for conjugation; and

recovering the conjugate exhibiting interferon β activity.

**60.** A pharmaceutical composition comprising a conjugate exhibiting interferon β activity and a pharmaceutically acceptable diluent, carrier, excipient or adjuvant.

**61.** The pharmaceutical composition of claim 60, wherein the pharmaceutical composition is effective for the treatment of one or more diseases.

**62.** The pharmaceutical composition of claim 61, wherein the pharmaceutical composition is effective for the treatment of multiple sclerosis.

**63.** A method for treating a mammal with multiple sclerosis comprising administering an effective amount of the pharmaceutical composition of claim 60.

**64.** A method for treating a mammal having circulating antibodies against interferon β 1a and/or 1b,which method comprises administering an effective amount of the pharmaceutical composition of claim 60.

**65.** The method of claim 63 or 64, wherein the mammal is a human.

**66.** A cell culture comprising

a) a host cell transformed with a nucleotide sequence encoding an interferon β polypeptide variant; and,

b) a culture medium.

**67.** The cell culture of claim 66, wherein the culture medium comprises an interferon β polypeptide variant produced by expressing the nucleotide sequence.

**68.** The cell culture of claim 67, wherein the concentration of the interferon β polypeptide variant is at least 800,000 IU/ml of medium.

**69.** The cell culture of claim 67, wherein the concentration of the interferon β polypeptide variant is in the range of 800,000-3,500,000 IU/ml medium.

**70.** A cell culture comprising a host cell of claim 53 or 55.

**71.** A method of producing an interferon β polypeptide variant, the method comprising:

(a) culturing a cell expressing an interferon β polypeptide variant in a culture medium, such that the concentration of the interferon β polypeptide variant in the medium is at least 800,000 IU/ml medium; and

(b) recovering the interferon β polypeptide variant.

**72.** The method of claim 71, wherein the concentration of the interferon β polypeptide variant is between 800,000 and 3,000,000 IU/ml medium.

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